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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/187,385	11/06/1998	SVETOMIR N. MARKOVIC	07039/119001	2986

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EXAMINER	
HOLLERAN, ANNE L	
ART UNIT	**PAPER NUMBER**
1642	16

DATE MAILED: 07/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/187,385	Applicant(s) MARKOVIC, SVETOMIR N.
	Examiner Anne Holleran	Art Unit 1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-6,8-12,18,21,22 and 26-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-6,8-12,18,21,22 and 26-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendment filed April 22, 2002 is acknowledged. Claims 27-40 were added.

2. Claims 4-6, 8-12, 18, 21, 22, 26 and 27-40 are pending and examined on the merits.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections Maintained:

4. The rejection of claims 4-6, 8, 18, 21, 22, and 26 under 35 U.S.C. 102(e) as being anticipated by Tovey et al (U.S. Patent 5,997,858; issued Dec. 7, 1999; filed May 9, 1997) is maintained and applied to new claims 39 and 40; the rejection of claims 9-12 under 35 U.S.C. 102(e) as being anticipated by Tovey et al in light of Brittenden et al (Brittenden, J. et al. Cancer, 77(7): 1226-1243, 1996, April) is maintained.

Claim 26 is drawn to a method for stimulating the immune system of a human patient having a non-resectable malignant tumor, comprising administering alpha-interferon to said patient, wherein the immunostimulatory dosage increases the natural killer lymphocyte ctyotoxicity of the patient by at least 50 percent above the baseline; and treating said patient with non-surgical medical methodologies to diminish said tumor. Thus, claim 26 appears to incorporate the limitations of claim 9. Claims 4-6, 39 and 40 recite ranges of dosages (500 U/m^2 to 500,00 U/m^2, 500 U/m^2 to 250,000 U/m^2, 500 U/m^2 to 1,000,000 U/m^2, 500 U/m^2 to 3,000,000 U/m^2, and 500 U/m^2 to 1,000,000 U/m^2). Claim 8 limits claim 26 to a dosage that is

administered once per day. Claims 18-22 limit the claimed methods to treatment of various cancers such as breast cancer, lung cancer, pancreatic cancer, brain cancer, prostate cancer, ovarian cancer, uterine cancer, renal cancer, and melanoma.

Applicant's arguments have been considered, but are unpersuasive. Because Tovey teaches methods using dosages that are within the range of those recited in claims dependent from claim 26, Tovey inherently teaches the methods of claim 26 and the methods of the claims dependent from claim 26. Furthermore, the ability of alpha-interferon to increase NK-lymphocyte activity is an inherent effect of the administration of alpha-interferon, as evidence by the teachings of Brittenden. Brittenden teaches that alpha-interferon enhances NK cell activity and has been successfully used in the treatment of renal carcinoma as part of a therapeutic regimen comprising the administration of interleukin-2 (see page 1234, 2nd column).

New Grounds of Rejection:

5. Claims 9 and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9 and 40 are indefinite because they recite limitations already present in claims 26 and 6, respectively.

6. Claims 27-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Markovic et al[a] (Markovic, S.N. et al, Int. J. Cancer, 45: 788-794, 1990; IDS ref. "CH") in view of Edwards et al (Edwards, B.S. et al., Cancer Research, 44; 3135-3139, 1984; cited in the IDS).

Claim 27 is drawn to a method for stimulating the immune system of a patient having a respectable tumor, comprising administering alpha-interferon to increasing the natural killer lymphocyte cytotoxicity by at least 50 percent above baseline; and surgically resecting the tumor. Dependent claims 28-38 add limitations to the dosages of alpha-inteferon and to the schedule of interferon administration. Claim 35 limits the cancer to various cancers. Claim 33 limits the increase in NK lymphocyte cytotoxicity to at least 75 percent above baseline. Claims 32 and 34 recite effector to target cell ratios of NK lymphocytes.

Markovic teaches that alpha-interferon acts to increase NK lymphocyte cytotoxicity and that this is a desired effect in the surgical treatment of cancer because of the presence of disseminated tumor foci following surgical excision of the primary tumor. Markovic also teaches a method for the surgical removal of a tumor in mice, where the mice were treated prior to surgery with alpha interferon. Markovic fails to teach the method in humans and fails to teach the dosages necessary to increase NK lymphocyte cytotoxicity by at least 50 percent or 75 percent. However, Edwards teaches dosages in humans that increase NK lymphocyte cytotoxicity by about 100 percent (see Table 4). The dose appears to be 1.65×10^6 U (see page 3136 and 3137, 15micrograms (1ng/ml = 110 units/ml)). Thus, it would have been prima facie obvious to one of skill in the art at the time the invention was made to have used the teachings of Markovic to make a method for treating humans by combining the teachings of Markovic with the teachings of Edwards.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

ALH

Anne L. Holleran
Patent Examiner
July 15, 2002

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